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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/578,744

06/20/2006

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EXAMINER

PIHONAK, SARAH

ART UNIT

PAPER NUMBER

1627

NOTIFICATION DATE

DELIVERY MODE

07/21/2010

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

sughrue@sughrue.com  
PPROCESSING@SUGHRUE.COM  
USPTO@SUGHRUE.COM

<b>Office Action Summary</b>	<b>Application No.</b> 10/578,744	<b>Applicant(s)</b> YOKOZAWA ET AL.	
	<b>Examiner</b> SARAH PIHONAK	<b>Art Unit</b> 1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 03 May 2010.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 10-17 and 19-23 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 10-17 and 19-23 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

This application is a national stage entry of PCT/JP04/17998, filed on 11/26/2004.

### **Priority**

This application claims foreign priority to 2003-398201, filed on 11/27/2003.

### **Response to Remarks**

1. Claims 10-17 and 19-22 were previously pending. In the response filed on 5/3/2010, Applicants added new claim 23, which has been included for examination in this office action.
2. Applicant's arguments filed 5/3/2010 have been fully considered but they are not persuasive. The Applicants have argued that the claims would not have been prima facie obvious to one of ordinary skill in the art, at the time of the invention, over Andersson et. al., in view of Saburi et. al., because Andersson et. al. teaches hydrogenation using H<sub>2</sub> as a donor, while Saburi et. al. teaches the use of alcohols as hydrogen donors. Therefore, the Applicants have asserted, one of ordinary skill in the art would not have been motivated to use the catalysts taught by Saburi for the asymmetric hydrogenation reaction taught by Andersson et. al. The examiner respectfully disagrees. Andersson et. al. teaches asymmetric hydrogenation to produce the instantly claimed phenylpropionic acids using a variety of catalysts, including chiral catalysts such as Rh-BINAP, or [Et-DuPHOS-Rh(COD)]. Saburi et. al. teaches that asymmetric hydrogenation reactions can be performed with chiral ruthenium complexes

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such as  $\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  or  $\text{Ru}_2\text{Cl}_4[(\text{R})\text{-H}_8\text{-binap}]_2\text{NEt}_3$ . As Rh-BINAP, [Et-DuPHOS-Rh(COD)],  $\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  and  $\text{Ru}_2\text{Cl}_4[(\text{R})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  are all transitional metal chiral complexes which are used for asymmetric hydrogenation reactions, and Andersson et. al. teaches that phenylpropionic acids can be successfully synthesized using transition metal chiral complexes, it would have been prima facie obvious, to one of ordinary skill in the art, at the time of the invention, to use complexes such as  $\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  and  $\text{Ru}_2\text{Cl}_4[(\text{R})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  to prepare such compounds. In response to the Applicants' argument that Andersson et. al. teaches  $\text{H}_2$  as a hydrogen donor while Saburi et. al. teaches alcohols as hydrogen donors, it is noted that Andersson et. al. does not exclude the presence of alcohols in the reaction. Additionally, while Saburi et. al. exemplifies the use of alcohols as hydrogen donors, it is well known in the art that asymmetric hydrogenation reactions have been performed with chiral transition metal catalysts using  $\text{H}_2$  as a donor. Furthermore, Saburi et. al. does not teach that the use of  $\text{H}_2$  as a donor would be unsuccessful for such reactions. Thus, as the use of  $\text{H}_2$  as hydrogen donor for asymmetric hydrogenation reactions is well known in the art, and as Andersson et. al. and Saburi et. al. teach that the chiral transition metal catalysts, Rh-BINAP, [Et-DuPHOS-Rh(COD)],  $\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  and  $\text{Ru}_2\text{Cl}_4[(\text{R})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  are used successfully for asymmetric hydrogenations, it would have been prima facie obvious to one of ordinary skill in the art to use  $\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  and  $\text{Ru}_2\text{Cl}_4[(\text{R})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  to prepare the phenylpropionic acids taught by Andersson et. al.

The Applicants have argued that the claimed reaction process was considered to be very challenging at the time of the invention, and have discussed the previously presented reference of Chen et. al. as support for this assertion. The Applicants have stated that Chen et. al. acknowledges that as of 2007, most known chiral diphosphine ligands with Rh resulted in low enantioselectivities and activities for the asymmetric hydrogenation of  $\alpha$ -substituted cinnamic acids. Additionally, the Applicants have also stated that the high % ee values obtained by Chen et. al. for the asymmetric hydrogenation were obtained by the use of TriFer, and not with the claimed chiral Ru complexes. While these arguments have been fully considered, they are not found persuasive. It is acknowledged that Chen et. al. teaches that asymmetric hydrogenation of  $\alpha$ -substituted cinnamic acids was considerably challenging; however, Andersson et. al. explicitly teaches that such a reaction can be successful. Andersson et. al. teaches that chiral transition metal complexes can be used to prepare phenylpropionic acids; therefore, as  $\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  and  $\text{Ru}_2\text{Cl}_4[(\text{R})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  are taught as chiral complexes useful for asymmetric hydrogenation reactions, one of ordinary skill in the art, at the time of the invention, would have been motivated to use such complexes to prepare phenylpropionic acids. The Applicants reference of Chemical and Engineering News, published on 10/27/2003, has also been fully considered. However, while this reference indicates that the preparation of phenylpropionic acids is challenging, this does not negate the teachings of Andersson et. al. As such, the rejection under 35 USC 103(a) was proper and is maintained, for reasons of record. For

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Applicants' convenience, this rejection will be reiterated below, with slight modification due to newly added claim 23. Accordingly, this action is made FINAL.

3. Claims 10-17, and 19-23 were examined.
4. Claims 10-17, and 19-23 are rejected.

### **Claim Rejections-35 USC § 103**

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

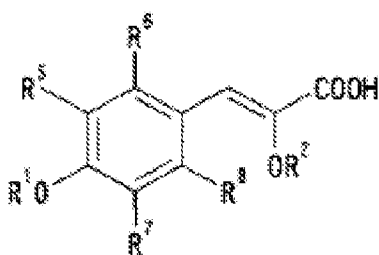
7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

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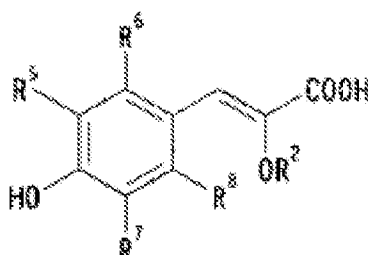
under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 10-17 and 19-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andersson et. al., US Patent No. 6,258,850, in view of Saburi et. al., US Patent No. 5,334,758 (both of previous record).

9. The instant claims are directed to a process for producing optically active phenyl propionic acids through asymmetric hydrogenation of the compounds of formula (4) and formula (9) as shown below:

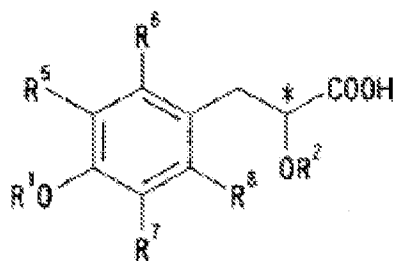


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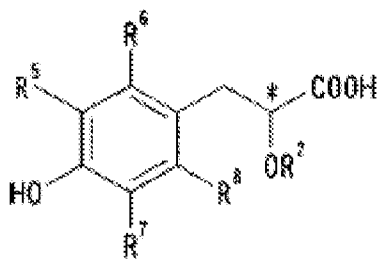


(9)

Where R<sup>1</sup>=protecting group; R<sup>2</sup>=alkyl group; R<sup>5</sup>-R<sup>8</sup>=H. The instant claims are also drawn to carrying out the hydrogenation in the presence of a chiral ruthenium complex, such as Ru<sub>2</sub>Cl<sub>4</sub>[(S)-H<sub>8</sub>-binap]<sub>2</sub>NEt<sub>3</sub> or Ru<sub>2</sub>Cl<sub>4</sub>[(R)-H<sub>8</sub>-binap]<sub>2</sub>NEt<sub>3</sub>, and that the resulting hydrogenated products, which are shown as compounds of formula (5) and (6) below, are further recrystallized after synthesis with solvents selected from hydrocarbons, alcohols, ketones, water, or mixtures thereof.

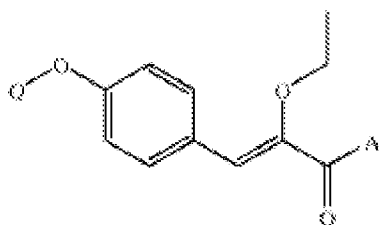


(5)

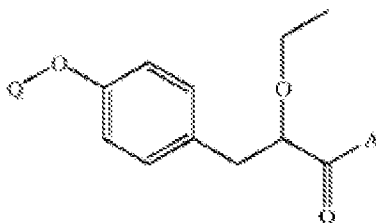


(6)

Andersson et. al. teaches that compounds of formula (VII) below can successfully undergo asymmetric hydrogenation to form compounds of formula (V), which is also shown below:



(VII)



(V)

Where  $A=\text{OH}$ ;  $Q=\text{H}$  or a protecting group (column 4, lines 29-46; column 7, line 50-column 8, line 24). The compounds taught by Andersson et. al. includes the compounds instantly claimed. Andersson et. al. teaches that the asymmetric hydrogenation reaction is conducted in the presence of chiral transition metal catalysts such as Rh-BINAP, [Et-DuPHOS-Rh(COD)], as well as a variety of other catalysts (column 8, lines 17-24). Crystallization of the products with solvents such as ethanol, isopropanol, and hydrocarbons and mixtures of solvents is taught (column 4, lines 66-67; column 13,



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lines 34-37; column 14, lines 42-45; column 15, lines 41-44). Andersson et. al. also teaches that the asymmetric hydrogenation can be performed in a wide variety of solvents (column 8, lines 25-32), and that protecting groups can be removed (column 5, lines 35-57).

While Andersson et. al. teaches that asymmetric hydrogenation can be successfully performed on compounds such as those instantly claimed, with chiral rhodium complexes and other metal catalysts, chiral ruthenium complexes such as  $\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  or  $\text{Ru}_2\text{Cl}_4[(\text{R})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  are not explicitly taught. It is not explicitly taught that the phenylpropionic acids are obtained at 58 % ee or greater.

Saburi et. al. teaches a process for preparing optically active carboxylic acids, through the asymmetric hydrogenation of  $\alpha$ ,  $\beta$ -unsaturated carboxylic acids with a chiral metal phosphine complex (Abstract). The metals used for the complex include ruthenium, rhodium, and palladium, with preference given to the ruthenium complexes of the formula shown below (column 2, line 64-column 3, line 6):



Where  $\text{R}^4=\text{H}$ , and  $\text{Y}$ =tertiary amine, such as triethylamine (column 3, lines 6-32). Saburi et. al. explicitly teaches that  $\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  or  $\text{Ru}_2\text{Cl}_4[(\text{R})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  are used to prepare optically active carboxylic acids (column 3, lines 41-43, and 56 and 58).

One of ordinary skill in the art, at the time of the invention, would have been motivated to use the complexes  $\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  or  $\text{Ru}_2\text{Cl}_4[(\text{R})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  taught by Saburi et. al., for the asymmetric hydrogenation of the compounds of formula (VII) taught by Andersson et. al., because Andersson et. al. teaches that such

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compounds can undergo asymmetric hydrogenation with chiral rhodium complexes, and Saburi et. al. teaches that  $\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  or  $\text{Ru}_2\text{Cl}_4[(\text{R})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  are used to catalyze the hydrogenation of  $\alpha$ ,  $\beta$ -unsaturated carboxylic acids with high stereoselectivity. As the compounds taught by Andersson et. al. are  $\alpha$ ,  $\beta$ -unsaturated carboxylic acids, one of ordinary skill in the art would have expected success in using complexes such as  $\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  or  $\text{Ru}_2\text{Cl}_4[(\text{R})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  to catalyze the asymmetric hydrogenation. Saburi et. al. also teaches that chiral rhodium complexes can be successfully used for the hydrogenation, but that preference is given to the ruthenium phosphine complexes. As such, it would have been prima facie obvious to replace the chiral rhodium complexes taught by Andersson et. al. with the chiral ruthenium complexes  $\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  or  $\text{Ru}_2\text{Cl}_4[(\text{R})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  for the asymmetric hydrogenation of compounds of formula (VII), with the expectation of improved optical purity. While it is not explicitly taught by Andersson et. al. or Saburi et. al. that the phenylpropionic acids are obtained at 58 % ee or greater, Saburi et. al. teaches that the use of chiral ruthenium complexes  $\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  and  $\text{Ru}_2\text{Cl}_4[(\text{R})\text{-H}_8\text{-binap}]_2\text{NEt}_3$  for asymmetric hydrogenations can produce products with % ee values up to 97% (columns 5 and 6, Tables 1, 2, and 3). Therefore, it would have been expected that similarly high % ee values would have been obtained for the phenylpropionic acids, when prepared with these catalysts.

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10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

### **Conclusion**

11. No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARAH PIHONAK whose telephone number is (571)270-7710. The examiner can normally be reached on Monday-Thursday 8:00 AM - 6:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

S.P.

/SREENI PADMANABHAN/  
Supervisory Patent Examiner, Art Unit 1627